

Antivirals - Hepatitis C Treatment

Medical policy no. 12.35.30.99

Effective August 1, 2019

Medical necessity

Drug	Medical Necessity
<u>Preferred</u> Glecaprevir/pibrentasvir (MAVYRET)	MAVYRET is preferred and covered without authorization.
<u>Non-preferred</u> Daclatasvir dihydrochloride (DAKLINZA) Elbasvir/grazoprevir (ZEPATIER) Ledipasvir/sofosbuvir (HARVONI) Ombitasvir/paritaprevir/ritonavir (TECHNIVIE) Ombitas/paritapr/riton and dasab pak (VIEKIRA) Sofosbuvir (SOVALDI) Sofosbuvir/velpatasvir (EPCLUSA) Sofosbuvir/velpatasvir/voxilaprevir (VOSEVI)	<p>All non-preferred antiviral products for the treatment of Hepatitis C virus (HCV) will be considered on a case-by-case basis.</p> <p>Non-preferred HCV antivirals may be considered medically necessary for the treatment of chronic HCV infection when Mavyret is not indicated <u>and</u> the clinical criteria listed below are met.</p> <p>Requests for brand-name medications with a generic equivalent available must also meet the criteria described in the Brands with Generic Equivalents policy (Non-Clinical Policy No. 0001).</p>

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
Daclatasvir dihydrochloride (DAKLINZA) Elbasvir/grazoprevir (ZEPATIER) Ledipasvir/sofosbuvir (HARVONI) Ombitasvir/paritaprevir/ritonavir (TECHNIVIE) Ombitas/paritapr/riton and dasab pak (VIEKIRA) Sofosbuvir (SOVALDI) Sofosbuvir/velpatasvir (EPCLUSA) Sofosbuvir/velpatasvir/voxilaprevir (VOSEVI)	<ol style="list-style-type: none"> 1. Patient has confirmed diagnosis of Hepatitis C and a quantifiable HCV RNA test >15 IU/mL within the last 12 months. 2. Required documentation and lab tests: <ol style="list-style-type: none"> a. HCV Genotype. b. Current HCV RNA Viral Load less than 12 months old. c. Fibrosis staging test (e.g. FibroScan® or FibroSURE®) to determine liver fibrosis level required to ensure the appropriate treatment regimen is used (e.g. patients with cirrhosis and/or decompensation may require longer treatment and/or ribavirin). Fibrosis staging test results must be less than 2 years old. d. Documentation of decompensation (or previous episodes of decompensation) if fibrosis level is F4 or cirrhosis. e. Documentation of treatment-experienced status including prior treatment regimen, length of treatment, response, and dates of treatment.

	<p>f. Lab reports, if available, documenting presence or absence of resistant mutations in treatment-experienced patients.</p> <p>3. Patients with the following conditions are not eligible for HCV treatment until the condition is resolved. Patients who:</p> <ol style="list-style-type: none"> Are taking medications that are contraindicated with or that have a severe drug interaction with the prescribed HCV treatment. Are pregnant or planning on becoming pregnant. Have severe end organ disease and are not eligible for transplantation (e.g. heart, lung, kidney) Have a clinically-significant illness or any other major medical disorder that may interfere with patients' ability to complete a course of treatment. In the professional judgment of the primary treating clinician, would not achieve a long-term clinical benefit from HCV treatment (e.g. patients with multisystem organ failure, receiving palliative care, with significant pulmonary or cardiac disease, or with malignancy outside of the liver not meeting oncologic criteria for cure). Have a MELD score <20 and one of the following: <ol style="list-style-type: none"> Cardiopulmonary disease that cannot be corrected and is a prohibitive risk for surgery Malignancy outside the liver not meeting oncologic criteria for cure Hepatocellular carcinoma with metastatic spread Intrahepatic cholangiocarcinoma Hemangiosarcoma Uncontrolled sepsis <p>Criteria (Reauthorization)</p> <p>See treatment experienced dosing guidelines below.</p>
--	--

Preferred therapies:

Drug Name	Preferred For:
Glecaprevir/pibrentasvir (MAVYRET)	<p>Patients with or without compensated cirrhosis (Child-Pugh A) that are:</p> <ul style="list-style-type: none"> treatment naïve patients with genotypes 1, 2, 3, 4, 5, and 6; or patients with genotypes 1, 2, 3, 4, 5, and 6 with prior treatment with peg-interferon, ribavirin, or sofosbuvir, but no prior treatment with an NS5A inhibitor or an NS3/4A protease inhibitor; or patients with genotype 1 with prior treatment with an NS5A inhibitor but not an NS3/4A protease inhibitor; or patients with genotype 1 with prior treatment with an NS3/4A protease inhibitor but not an NS5A inhibitor.

Sofosbuvir/velpatasvir (EPCLUSA) Sofosbuvir/velpatasvir/voxilaprevir (VOSEVI)	Will be considered on a case-by-case basis when treatment with Mavyret is not indicated.
--	--

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
Glecaprevir/pibrentasvir (MAVYRET)	<p>Treatment Naïve Genotypes 1, 2, 3, 4, 5, 6</p> <ul style="list-style-type: none"> 8 weeks without cirrhosis 12 weeks with compensated cirrhosis <p>Treatment Experienced</p> <ul style="list-style-type: none"> With peg-interferon, ribavirin, or sofosbuvir, but no prior treatment with an NS5A inhibitor or an NS3/4A protease inhibitor <ul style="list-style-type: none"> Genotypes 1, 2, 4, 5, 6 <ul style="list-style-type: none"> 8 weeks without cirrhosis 12 weeks with compensated cirrhosis Genotype 3 <ul style="list-style-type: none"> 16 weeks with or without compensated cirrhosis With an NS5A inhibitor without an NS3/4A protease inhibitor <ul style="list-style-type: none"> 16 weeks for Genotype 1 with or without compensated cirrhosis With an NS3/4A protease inhibitor without an NS5A inhibitor <ul style="list-style-type: none"> 12 weeks for Genotype 1 with or without compensated cirrhosis
Sofosbuvir/velpatasvir (EPCLUSA) Sofosbuvir/velpatasvir/voxilaprevir (VOSEVI)	Will be determined on a case-by-case basis when treatment with Mavyret is not indicated.

References

- American Association for the Study of Liver Disease (AASLD). Recommendations for testing, managing, and treating Hepatitis C. 2014; Available at: <http://www.hcvguidelines.org/full-report-view>. Accessed January 14, 2014.
- Fabrizi F, Martin P, Dixit V, Messa P. Meta-analysis of observational studies: Hepatitis C and survival after renal transplant. *J of Viral Hepas*. 2014; 21: 314-324.
- Berenguer M, Schuppan D. Progression of liver fibrosis in post-transplant Hepatitis C: mechanisms, assessment, and treatment. *J Hepatol*. 2013; 58: 1028-1041.
- Curry MP, Forns X, Chung RT, et al. Sofosbuvir and ribavirin prevent recurrence of HCV infection after liver transplantation: An open-label study. *Gastroenterology*. 2015; 148: 108-17.
- Flamm SL, Everson GT, Charlton MR, Denning JM, Arterburn S, Brandt-Sarif T. Ledipasvir/Sofosbuvir with ribavirin for the treatment of HCV in patients with decompensated cirrhosis: Preliminary results of a prospective, multicenter study. 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at: http://www.natap.org/2014/AASLD/AASLD_36.htm.
- Dove LM, Brown RS. Liver transplantation in adults: Patient selection and pretransplantation valuation. In: UpToDate, Post TW (Ed), UpToDate, Waltham, MA. (Accessed on December 4, 2014.)
- Gilead Science. Sofosbuvir (Sovaldi™). Product Label. 2014. Accessed January 20, 2015.
- Gilead Science. Ledipasvir/Sofosbuvir (Harvoni™). Product Label. 2014. Accessed January 20, 2015.

9. AbbVie. Ombitasvir/Paritaprevir/Ritonavir/Dasabuvir (Viekira Pak™). Product Label. 2014. Accessed January 20, 2015.
10. Kowdley K, Gordon S, Reddy R, et al. Ledipasvir and sofosbuvir for 8 or 12 weeks for chronic HCV without cirrhosis (ION3). *N Engl J Med*. 2014; 370: 1879-88.
11. Feld JJ, Kowdley KV, Coakley E, et al. Treatment of HCV with ABT-450/r/ombitasvir and dasabuvir and ribavirin (SAPPHIRE-I). *N Engl J Med*. 2014; 370: 1594-1603.
12. Zeuzem S, Jacobson IM, Baykal T, et al. Retreatment of HCV with ABT-450/r-ombitasvir and dasabuvir with ribavirin (SAPPHIRE-II). *N Engl J Med*. 2014; 370: 1604-1614.
13. Ferenci P, Berstein D, Lalezari J, et al. ABT-450/r-ombitasvir and dasabuvir with or without ribavirin for HCV (PEARL-III/IV). *N Engl J Med*. 2014; 370: 1983-1992.
14. Afdhal N, Zeuzem S, Kwo P, et al. Ledipasvir and sofosbuvir for untreated HCV genotype 1 infection (ION1). *N Engl J Med*. 2014;370: 1889-98.
15. Poordad F, Hezode C, Trinh R, et al. ABT-450/r-ombitasvir and dasabuvir with ribavirin for Hepatitis C with cirrhosis (TURQUOISE-II). *N Engl J Med*. 2014; 370: 1973-1982.
16. Afdhal N, Reddy R, Nelson D, et al. Ledipasvir and sofosbuvir for previously treated HCV Genotype 1 Infection (ION2). *N Engl J Med*. 2014; 370: 1483-93.
17. Bourlier M, Sulkowski M, Omata M, et al: An integrated safety and efficacy analysis of > 500 patients with compensated cirrhosis treated with ledipasvir/sofosbuvir with or without ribavirin. 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at: http://www.natap.org/2014/AASLD/AASLD_15.htm.
18. Andreone P, Colombo MG, Enejosa JV, et al. ABT-450, ritonavir, ombitasvir, and dasabuvir achieves 97% and 100% sustained virologic response with or without ribavirin in treatment-experienced patients with HCV genotype 1b infection (PEARL-II). *Gastroenterology*. 2014; 147:359-365.
19. Jacobson I, Gordon S, Kowdley K, et al. Sofosbuvir for Hepatitis C genotype 2 or 3 in patients without treatment options (POSITRON/FUSION). *N Engl J Med*. 2013; 368: 1867-1877.
20. Zeuzem S, Dusheiko G, Salupere R, et al. Sofosbuvir and ribavirin in HCV genotypes 2 and 3 (VALENCE). *N Engl J Med*. 2014; 370: 1993-2001.
21. Lawitz E, Poordad F, Brainard D, et al. Sofosbuvir with Peginterferon-ribavirin for 12 weeks in previously treated patients with Hepatitis C genotype 2 and 3 and cirrhosis. *Hepatology*. 2014 doi: 10.1002/hep.27567.
22. Gane EJ, Stedman CA, Hyland RH, et al. Nucleotide polymerase inhibitor sofosbuvir plus ribavirin for Hepatitis C (ELECTRON). *N Engl J Med*. 2013; 368:34-44.
23. Gane E, Hyland R, An D, et al. Ledipasvir/Sofosbuvir fixed-dose combination is safe and effective in difficult-to-treat populations including GT3 patients, decompensated GT1 patients, and GT1 patients with prior sofosbuvir experience. International Liver Congress. 2014. London UK.
24. Gane EF, Hyland RH, An D, et al. High efficacy of LDV/SOF regimens for 12 weeks for patients with HCV genotype 3 or 6 infection. . [Abstract LB11.] 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at: http://www.natap.org/2014/AASLD/AASLD_27.htm.
25. Lawitz E, Mangia A, Wyles D, et al. Sofosbuvir for previously untreated chronic Hepatitis C infection (FISSION/NEUTRINO). *N Engl J Med*. 2013; 368: 1878-1887.
26. Ruane PJ, Ain D, Riad J, et al. Sofosbuvir plus ribavirin in the treatment of chronic HCV genotype 4 infection in patients of Egyptian ancestry. 64th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 1-4, 2013. Washington DC.
27. Kapoor R, Kohli A, Sidharthan S, et al. All oral treatment for genotype 4 chronic Hepatitis C infection with sofosbuvir and Ledipasvir: Interim results from the NIAID SYNERGY trial. [Abstract 240.] 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at http://www.natap.org/2014/AASLD/AASLD_76.htm.

28. Pol S, Reddy KR, Baykal T et al. Interferon-free regimens of ombitasvir and ABT-450/r with or without ribavirin in patients with HCV genotype 4 infection: PEARL-I study results. [Abstract 1928.] 65th Annual Meeting of the American Association for the Study of Liver Diseases (AASLD). November 7-11, 2014; Boston, MA.
29. Sulkowski MS, Naggie S, Lalezari J, et al. Sofosbuvir and ribavirin for Hepatitis C in patients with HIV coinfection (PHOTON-I). *JAMA*. 2014; 312(4): 353-361.
30. Molina JM, Orkin C, Iser DM, et al. Sofosbuvir plus ribavirin for the treatment of Hepatitis C infection in patients coinfecting with HIV (PHOTON-2): A multicenter, open label, nonrandomized, phase 3 study. *Lancet*. Published online February 4, 2015. Accessed February 16, 2015.
31. Townsend K, Osinusi A, Nelson A, et al. Use of Ledipasvir/sofosbuvir fixed dose combination for treatment of HCV genotype-1 infection in patients coinfecting with HIV (ERADICATE). [Abstract 84.] 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at: http://www.natap.org/2014/AASLD/AASLD_01.htm.
32. Wyles D, Sulkowski MS, Eron JJ, et al. TURQUOISE-I: 94% SVR12 in HCV/HIV-1 coinfecting patients treated with ABT-450/r/ombitasvir and dasabuvir and ribavirin. [Abstract 1939.] 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at: http://www.natap.org/2014/AASLD/AASLD_28.htm.
33. Charlton M, Gane E, Manns MP, et al. Sofosbuvir and ribavirin for treatment of compensated recurrent Hepatitis C virus infection after liver transplantation. *Gastroenterology*. 2014; doi:10.1053/j.gastro.2014.10.001.
34. Reddy KR, Everson GT, Flamm SL, Denning JM, Arterburn S, Brandt-Sarif T. Ledipasvir/Sofosbuvir with ribavirin for the treatment of HCV in patients with post-transplant recurrence: Preliminary results of a prospective, multicenter study. [Abstract 8.] 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at http://www.natap.org/2014/AASLD/AASLD_16.htm.
35. Kwo PY, Mantry PS, Coakley E, et al. An interferon-free antiviral regimen for HCV after liver transplantation (CORAL-I). *N Engl J Med*. 2014; 371: 2375-2382.
36. Flamm SL, Everson GT, Charlton MR, et al. Ledipasvir/sofosbuvir with ribavirin for the treatment of HCV in patients with decompensated cirrhosis: Preliminary results of a prospective multicenter study. 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014. Boston, MA. Available at http://www.natap.org/2014/AASLD/AASLD_36.htm.
37. Bristol-Myers-Squibb. Daclatasvir (Daklinza™). Product Label 2015. Accessed August 12, 2015.
38. AbbVie. Ombitasvir/Paritaprevir/Ritonavir/ (Technivie™). Product Label 2015. Accessed August 12, 2015.
39. Nelson DR, Cooper JN, Lalezari JP, et al. All-Oral 12-Week 12-week treatment with daclatasvir plus sofosbuvir in patients with hepatitis C virus genotype 3 infection: ALLY-3 phase III study. *Hepatology*. 2015; 61: 1127-1135.
40. Hézode C, Asselah T, Reddy KR, et al. Ombitasvir plus paritaprevir plus ritonavir with or without ribavirin in treatment-naïve and treatment-experienced patients with genotype 4 chronic hepatitis C virus infection (PEARL-I): a randomized, open-label trial. *Lancet*. 2015; 385: 2502-2509.
41. Sulkowski MS, Gardiner DF, Rodriguez-Torres M, et al. Daclatasvir plus sofosbuvir for previously treated or untreated chronic HCV infection. *NEJM*. 2014; 370(3): 211-221.
42. Jacobson IM, Dore GH, Fried MW, et al. Simeprevir with pegylated interferon alfa 2a plus ribavirin in treatment-naïve patients with chronic hepatitis C virus genotype 1 infection (QUEST-1): a phase 3, randomized, double-blind, placebo-controlled trial. *Lancet*. 2014; 384: 403-413.
43. Manns M, Marcellin P, Poordad F, et al. Simeprevir with pegylated interferon alfa 2a or 2b plus ribavirin in treatment-naïve patients with chronic hepatitis C virus genotype 1 infection (QUEST-2): a randomized, double-blind, placebo-controlled, a phase 3 trial. *Lancet*. 2014; 384: 414-426.

44. Lawitz E, Poordad F, Brainard DM, et al. Sofosbuvir with peginterferon-ribavirin for 12 weeks in previously treated patients with Hepatitis C and genotype 2 or 3 and cirrhosis. *Hepatology*. 2015; 61: 769-775.
45. Foster GR, Pianko S, Brown A, et al. Efficacy of sofosbuvir plus ribavirin with or without peginterferon-alfa in patients with hepatitis C virus genotype 3 infection and treatment-experienced patients with cirrhosis and hepatitis C virus genotype 2 infection. *Gastroenterology*. 2015; 1-9. doi: 10.1053/j.gastro.2015.07.043.
46. Doss W, Shiha G, Hassany M, et al. Sofosbuvir plus ribavirin for treating Egyptian patients with hepatitis c genotype 4. *J Hepatology*. 2015; 63: 581-585.
47. Ruane PJ, Ain D, Stryker R, et al. Sofosbuvir plus ribavirin for the treatment of chronic genotype 4 hepatitis C virus infection in patients with Egyptian ancestry. *J Hepatology*. 2015; 62: 1040-1046.
48. Kohli A, Kapoor R, Sims Z, et al. Ledipasvir and sofosbuvir for hepatitis C genotype 3: a proof-of-concept, single centre, open-label phase 2a cohort study. *Lancet*. 2015; 15: 1049-1054.
49. Kwo P, Gitlin N, Nahass R, et al. A phase 3, randomized, open-label study to evaluate the efficacy and safety of 8 and 12 weeks fo Simeprevir (SMV) plus sofosbuvir (SOF) in treatment-naïve and experienced patients with chronic HCV genotype 1 infection without cirrhosis: OPTIMIST-1. 50th Annual Meeting of the European Association for the Study of the Liver (EASL). April 22-26, 2015; S270; Vienna, Austria.
50. Abergel A, Loustaud-Ratti V, Mitivier S, et al. Ledipasvir/sofosbuvir for the treatment of patients with chronic genotype 4 or 5 HCV infection. 50th Annual Meeting of the European Association for the Study of the Liver (EASL). April 22-26, 2015; Vienna, Austria.
51. Foster GR, McLauchlan J, Irving W, et al. Treatment of decompensated HCV cirrhosis in patients with diverse genotypes: 12 weeks sofosbuvir and NS5A inhibitors with/without ribavirin is effective in HCB genotypes 1 and 3. [Abstract O002] 50th Annual Meeting of the European Association for the Study of the Liver (EASL). April 22-26, 2015; Vienna, Austria. Available at http://natap.org/2015/EASL/EASL_34.htm
52. Wyles DL, Ruane PJ, Sulkowski MS, et al. Daclatasvir plus sofosbuvir for HCV in patients coinfectd with HIV-1. *NEJM*. 2015; 373(8): 714-725.
53. Poordad F, Schiff ER, Vierling JM, et al. Daclatasvir, sofosbuvir, and ribavirin combination for HCV patients with advanced cirrhosis or post-transplant recurrence: ALLY-1 phase 3 study. [Abstract L08] 50th Annual Meeting of the European Association for the Study of the Liver (EASL). April 22-26, 2015; Vienna, Austria.
54. Bourliere M, Bronowicki J, de Ledinghen V, et al. Ledipasvir/sofosbuvir fixed dose combination is safe and efficacious in cirrhotic patients who have previously failed protease-inhibitor based triple therapy. [Abstract LB-6.] 65th annual Meeting of the American Association for the Study of Liver Diseases (AASLD). November 7-11, 2014; Boston, MA.
55. Charlton M, Everson GT, Flamm SL, et al. Ledipasvir and sofosbuvir plus ribavirin for treatment of HCV infection in patients with advanced liver disease. *Gastroenterology*. 2015; 149: 649-659.
56. Pungpapong S, Werner KT, Aqel B, et al. Multicenter experience using sofosbuvir and Simeprevir with/without ribavirin to treat HCV genotype 1 after liver transplantation. [Abstract 9] 65th Annual Meeting of the American Association for the Study of Liver Disease (AASLD). November 7-11, 2014; Boston, MA.
57. Pockros PJ, Reddy KR, Mantry PS, et al. Safety of ombitasvir/paritaprevir/ritonavir plus dasabuvir for treating HCV GT1 infection in patients with severe renal impairment or end-stage renal disease: the RUBY-1 study. [Abstract L01] 50th Annual Meeting of the European Association for the Study of the Liver (EASL). April 22-26, 2015; Vienna, Austria.
58. Merck. Elbasvir/grazoprevir (Zepatier™) Product Label. 1/2016. Accessed June 6, 2016.
59. Gilead. Sofosbuvir/velapatasvir (Epclusa®) Product Label. 6/2016. Accessed September 9, 2016.
60. Abbvie. Glecaprevir/pibrentasvir (Mavyret™) Product Label. 8/2017. Accessed November 2, 2017.

History

Date	Action and Summary of Changes
06-07-2019	<ul style="list-style-type: none"> Updated policy for preferred therapies and formatting.

07-08-2019	<ul style="list-style-type: none"> Placed in updated policy format Removed prescriber specialty requirement Removed proof of chronic HCV infection Added all drugs to the policy Mavyret only preferred agent Added treatment regimens
07-23-2019	Updated policy to reflect Mavyret covered without authorization
08-14-2019	Removed Mavyret from initial approval criteria